Allergic reactions in the middle and inner ear

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Allergy can affect the outer, the middle, and the inner ear. The incidence of allergy in the production of middle and inner ear symptoms continues to be controversial. Controversy also exists as to where the anatomic target organ of an allergy reaction capable of producing a middle ear effusion would lie. Data continue to accumulate that suggest that patients with Meniere's disease and allergies treated with specific methods of allergy immunotherapy and/or dietary avoidance will have an improved clinical outcome for their Meniere's disease. Objective diagnostic tests, including electrocochleography, have shown promise when combined with allergy testing modalities in helping to identify those patients with Meniere's disease who may have an allergic etiology for their symptoms. This article reviews the role that allergic disease may play in the production of middle and inner ear symptoms. Curr Opin Otolaryngol Head Neck Surg 2000, 8:245–248 © 2000 Lippincott Williams & Wilkins, Inc.

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Abbreviations

OME	otitis media with effusion
ELISA	enzyme-linked immunosorbent assay

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Approximately 20% of Americans suffer from hypersensitivity diseases. The head and neck are the most commonly affected target organs of the allergic reaction, and the effect of allergic reactions in producing nasal symptoms was first reported by Dr. French K. Hansel [1].

The ear also has been suspected of serving as a target organ for an allergic reaction. In fact, the first case report suggesting an allergic basis for labyrinthine symptoms was published in 1893, and Duke published the first clinical report of a suspected allergic etiology for Meniere's disease in 1923 [2,3]. Likewise, anecdotal information about an allergic basis for otitis media with effusion and other middle ear disorders has been reported for generations.

This chapter reviews the immune and allergic activity of the ear as we currently understand it and discusses various treatment modalities to address the underlying allergic pathogenesis. Allergy may affect the external ear, middle ear, and/or labyrinth (Table 1). This chapter will focus on the role that allergy plays in diseases of the middle and inner ear and will review current literature pertaining to these areas.

Middle ear

Ear fullness is one of the most common presenting symptoms in an otologic practice. This symptom alone is certainly not diagnostic and may indicate problems within the external, middle, or inner ear. The typical causes of external ear pathology resulting in a symptom of fullness are generally quite obvious on the physical examination. Objective tests, such as audiograms, tympanometry, or eustachian tube function testing generally will help distinguish between fullness presenting as a middle ear symptom and that of labyrinthine origin.

A relation among upper respiratory tract infections, allergy, and resulting poor eustachian tube function long has been recognized. Allergy may play a role not only in eustachian tube dysfunction, but, in some cases, may result in a patulous eustachian tube as well. The ear fullness secondary to eustachian tube dysfunction can result in diverse symptoms, ranging from minor annoyance to loss of employability.

Eustachian tube dysfunction has been shown to result after provocative intranasal challenges with pollen, house dust mite, and histamine [5–8]. Howard *et al.* [9]

Table 1. Otologic manifestations of allergy

External ear
Chronic external otitis (COE)
Sensitization to otic drops
Contact sensitivity (hearing aid ear molds, nickel)
Dermatophytid reaction to fungal infection
Red auricle (vasodilation to foods)
Middle ear
Eustachian tube dysfunction
Patulous eustachian tube
Otitis media with effusion (OME)
Chronic otitis media/draining ear
Inner ear
Meniere's disease
Vestibular hydrops
Cochlear hydrops
Dizziness
Tinnitus

From [4], with permission.

described the efficacy of a screening radioallergosorbent test (RAST) in the diagnosis of eustachian tube function, as well as other middle and inner ear disorders.

The role of allergy in the production of eustachian tube dysfunction has not been as commonly evaluated as it has in the suspected production of otitis media with effusion (OME). We studied 151 patients with eustachian tube dysfunction who had evidence of allergy and underwent allergy testing and treatment [10]. Of these patients, 92.3% were positive to one or more foods, and all had reactivity to inhalant allergens. Nearly all had used one or more other treatments without success before allergy therapy. After treatment with immunotherapy or diet, fullness was rated as improved in 71% of patients, with allergy symptoms and well being improved in 83% and 80% of patients, respectively. Statistically, the most significant predictive factor of success in the treatment of ear fullness in this patient population was adherence to recommended elimination diet in those who were diagnosed with food allergies. We also found improvement in refractory cases of patulous eustachian tube dysfunction treated with immunotherapy or diet.

Otitis media with effusion

Otitis media with effusion is the most common cause of hearing loss in children today. The published incidence of allergy in OME has been reported to range from 0 to more than 95% [11]! Many would agree that neuromuscular immaturity of the eustachian tube is involved in a large percentage of OME cases. The most controversial areas dealing with allergic OME are defining the true incidence, defining the anatomic site of the target organ, and determining what treatment modality is most efficacious. We shall discuss each of these.

The variability in the reported prevalence of an allergic etiology for OME largely reflects the controversy and strongly held opinions of different investigators, coupled with the known different sensitivity levels of skin test techniques used for testing. Also, food allergens, which have been shown to be a significant factor in the production of allergic symptoms in children younger than 2 years old often are not included in the testing panel in many reported case series. Although it is impossible in this text to review all of the case histories and outcome studies on skin testing and *in vitro* results, we believe that in recent literature the most valid conservative estimate of allergic incidence would be 35%, as reported by Bernstein [12]. He used a combination of *in vitro* and prick testing, which, although less sensitive than serial endpoint titration (SET), would certainly, in combination, be expected to show high specificity for the diagnosis of antigen-specific IgE-mediated allergy. He was of the opinion that food allergies did not play a significant role in the production of allergic eustachian tube dysfunction, which is counter to the experience in the adult patients reported by this author. His testing technique was specifically for IgE-mediated disease, however, whereas many of us who practice clinical allergy are of the feeling that non-IgE mediated reactions may play a significant role in the production of symptoms produced by food ingestion.

The anatomic site of reaction capable of producing the symptoms of OME must, by necessity, be one or a combination of the following: the nose, eustachian tube, and proximal nasopharynx, or the middle ear itself. The reader is encouraged to read the excellent review by Bernstein of various studies that have been performed to try to delineate exactly where the anatomic pathology occurs [12]. He concludes that the most likely site of an immune reaction capable of ultimately producing an effusion in the middle ear space would be the eustachian tube itself, specifically at its nasopharyngeal end. He reminds us that the edema resulting from a localized immune reaction in this area anatomically impairs the function of the tensor villi palatini (TVP) muscle, ultimately resulting in the production of a middle ear effusion.

Although Bernstein [12] reported that evidence of the middle ear itself as target organ of an allergic reaction is less than 8%, the literature this year had some interesting conclusions of a different nature by Hurst *et al.* [13••,14•]. Hurst *et al.* evaluated 18 atopic children by micro-ELISA and found an elevation in antigen-specific IgE in the middle ear effusion in 83%. Of 214 antibodies measured in the serum, however, only 30% were found in the middle ear effusion. They concluded that it was unlikely that the high percentage of antigen-specific IgE found in the middle ear was a result of passive transfer from plasma and that the middle ear itself was likely the target organ of an active Th2

immunologic response as has been described by Johnson *et al.* [15].

Hurst *et al.* also reported on the presence of tryptase, a mast cell mediator, in the chronic middle ear effusion of atopic patients [14•]. Although they argued that this gives further credence to the supposition that the middle ear itself is the site of allergic reaction producing OME, it has been shown that mast cell activity is increased in chronic inflammatory reactions, whether or not atopy is involved [16,17]. It is this author's opinion that it is more likely that the pathology occurs in the proximal eustachian tube and nasopharynx, although there may well be a higher incidence of direct involvement of the middle ear mucosa than has been previously reported.

Despite the lack of agreement as to where the most likely target organ of an allergic reaction producing a middle ear effusion occurs, what is less controversial is what the most appropriate treatment modalities would be. Cantekin *et al.* [18] have shown, in a study of a large number of children with OME, that the use of antihistamines is not efficacious in the resolution of the effusion.

Since Cantekin *et al.*'s publication, several third generation nonsedating antihistamines have been released for patient use. Suzuki *et al.* [19•] reported on the efficacy of one of these newer medications, Azelastine hydrochloride (AZ), in the animal model for the evacuation of a middle ear effusion. They found on histopathologic study that inflammation in the nasopharynx and at the tubal orifice was quite prominent and concluded, as had Bernstein, that an allergic involvement of the eustachian tube itself was responsible for the ultimate production of a middle ear effusion. They also found that AZ administration facilitated the elimination of a middle ear effusion in guinea pigs who had simultaneous OME and allergic rhinitis. They did not find evidence that AZ was useful for presumed nonallergic reactions resulting in the release of histamine from mast cells and leukocytes.

Suzuki *et al.* [20•] then reported on a subsequent study assessing the clinical efficacy of AZ in the human with OME. Although treated patients clearly had an improvement in their nasal symptoms, there was no improvement in the resolution of the middle ear effusion.

At the present time, it would appear that the best treatment outcomes in allergic middle ear disease are produced by the use of specific allergy immunotherapy after testing with either SET or *in vitro* techniques and an elimination of significant food antigens from the diet [4].

Inner ear

Endolymphatic hydrops is found in many conditions other than Meniere's disease, including infections (otosyphilis, labyrinthitis, and meningitis) and autoimmune diseases (Cogan's), as well as otosclerosis and after head trauma. It is most likely that Meniere's disease is multifactorial in nature, requiring an underlying predisposition, such as a genetic factor, an anatomic variant such as a small endolymphatic sac or other abnormality, and then secondarily requiring a triggering event to develop classical symptoms.

Ruckenstein, [21•] in a review of immunologic factors in Meniere's disease, discussed the association of HLA antibodies with Meniere's disease. He noted the disparity between the observed pathologic changes in Meniere's disease and those seen in other immune-mediated labyrinthine or cochlear diseases. He concluded that more subtle immune abnormalities must be taking place.

Ruckenstein discussed the possible role of allergy in the production of Meniere's disease, but concluded that this area has not been thoroughly evaluated and that there have not been clinical trials. He further concluded that reported improvement in allergic Meniere's disease patients may well be attributed to the vestibular suppressing effects of the sedating antihistamines with which they are frequently treated.

In contrast, this author has two new articles in press dealing with allergic Meniere's disease. In one, a control group of patients with Meniere's disease and allergy who did not undergo treatment with allergy immunotherapy or diet are compared with those who did. There was a significant difference in outcome between these two groups, with the allergy treatment patients doing much better in all aspects pertaining to their Meniere's disease [22]. Of note, 41% of those patients who were treated with allergy therapy were able to stop all of their other medications, including any vestibular suppressing antihistamines. In a second paper to be published this year, we reported that the prevalence rate of allergy in patients with Meniere's disease is 40%, which is twice as high as that reported in the general population [23].

Probably the most interesting recent publication about Meniere's disease was that by Gibbs *et al.*, [24••] where electrocochleographic changes were noted in patients with known inhalant allergy and Meniere's disease. Most references in the literature to objective studies on Meniere's patients with suspected allergy (audiograms, electrocochleography, electronystagmography, etc.) have dealt with the effects of challenge with food antigens. Although it has been reported that the prevalence of

suspected airborne triggers of Meniere's disease is slightly higher than that of food allergens, this was the first study demonstrating an objective finding of affected summating potential abnormalities after nasal inhalation of inhalant antigens.

Unfortunately, no new information was published this year about the roles of allergy either in the production of tinnitus or cochlear hydrops.

Conclusion

Allergy may affect the outer, middle, or inner ear. The site of an allergic reaction capable of producing a middle ear effusion continues to be controversial, but it would appear that the most efficacious form of treatment for allergic middle ear disease is antigen-specific immunotherapy and dietary elimination of suspected food allergens.

The prevalence rate of allergy in patients with Meniere's disease appears to be much higher than has been reported for the general population. Electrocochleography has been shown to give objective evidence of abnormalities in summating potential in patients with allergy and Meniere's disease undergoing intranasal challenge with inhalant allergens.

References and recommended reading

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